

Claims

1. A recombinant nematode nicotinic receptor comprising the amino acid sequence set forth in SEQ ID No.:1.
2. An isolated DNA which encodes a *C.elegans unc-63* α nAChR subunit, which subunit is a functional nematode nicotinic receptor, comprising the amino acid sequence of SEQ ID No. 1.
3. A DNA segment according to claim 2 which is a cDNA comprising the amino acid sequence of SEQ ID No.:1 .
4. A vector containing the DNA of claim 2.
5. A host transformed by the vector of claim 4.
6. A host containing a transgene encoding a recombinant receptor according to claim 1.
7. A host according to claim 6 which is a cell line.
8. A method of producing a recombinant nematode nicotinic receptor having the amino acid sequence set forth in SEQ ID No.:1 comprising culturing a host cell according to claim 6 under conditions which permit the expression of said receptor.
9. A method according to claim 8 in which the *C.elegans unc-63* gene which encodes α nAChR subunit is coexpressed with one or more nAChr subunits.

10. A method of screening for antihelminthic compounds which includes the steps of:
- i) exposing a recombinant receptor according to claim 1 to a compound to be screened for antihelminthic activity;
 - ii) selecting a compound which interacts with said receptor; and
 - iii) characterising said selected compound as an antihelminthic compound.
11. A method of controlling parasitic nematode growth in a host , which comprises the administration of :
- i) exposing a recombinant receptor according to claim 1 to a compound to be screened for antihelminthic activity;
 - ii) selecting a compound which interacts with said receptor; and
 - iii) characterising said selected compound as an antihelminthic compound.
12. A recombinant nematode nicotinic receptor according to claim 1 which mimics the response of the natural receptor to the antihelminthic drug Levamisole.

Abstract

Recombinant Nematode Nicotinic Receptor and Uses

We describe the molecular and functional characterization of the *C. elegans unc-63* gene, a levamisole resistance locus on chromosome I, which encodes a nicotinic acetylcholine receptor (nAChR) α subunit. The derived amino acid sequence of UNC-63 most closely resembles that of UNC-38, the product of a separate levamisole resistance locus. Using a gfp::*unc-63* fusion construct, expression has been detected in muscles (body wall, vulval) and motoneurons of *C. elegans*. Nuclear injection into *Xenopus laevis* oocytes of *unc-63* cDNA together with *lev-1* and *unc-29* results in the expression for the first time of a robust functional *C. elegans* heteromeric nAChR. The EC₅₀ for ACh of the expressed receptor (20 μ M) resembles that of native nematode muscle nAChRs. Nicotine and the anthelmintic drug levamisole are agonists and mecamylamine is an antagonist of this expressed receptor. When *unc-38* cDNA is co-injected with cDNAs encoding *unc-63*, *lev-1* and *unc-29* much smaller amplitude agonist-activated currents are observed. The first robust functional recombinant heteromeric nAChR composed only of invertebrate subunits has therefore been characterized and shown to contain a pesticide binding site.